REMARKS

Claims 28-31 are pending in the application. Claims 12-27 are canceled. Applicants reserve the right to prosecute these claims and other claims in this application and other applications.

Claims 28-31 are rejected under 35 USC § 103(a) as being unpatentable over Forsythe et al. (U.S. Patent No. 4,214,993) ("Forsythe"), Sauer et al. (EP 0969090) ("Sauer") and Hansen et al. (U.S. Patent No. 6,672,458) ("Hansen"). This rejection is respectfully traversed.

The claimed invention relates to a particular process of sucking/discharging of a nucleic acid containing solution into/out of a tip using a pumping means that is designed to cause pressure change for the sucking/discharging action (see, e.g., ¶[0034] of the specification, in which sucking/discharging is provided typically by a syringe pump). As noted in the specification, "in a sucking/discharging method, washing solution tends to remain within the solid phase used in a purifying or analyzing device and such remaining washing solution badly influences on the performance of a nucleic acid analysis." Thus, an important aspect of the invention is the use of the air-blowing technique to remove the remaining washing solution left off within the solid phase in the sucking/discharging method.

This remaining washing solution problem originates in the use of a solid phase with a low flow-through resistance in the sucking method, to allow the nucleic acid containing sample to easily flow through the solid phase. For example, an embodiment of the present invention uses a device that comprises blocking members 40a and 40b, the members being porous enough to permit liquid or gas to easily flow therethrough and powdered flint glass is filled between them.

Forsythe relates to a method of separating, by centrifugal force, components such as blood or urine together with spherical porous supports. Sauer relates to a method of recovering, by a spin column, nucleic acid using silica-gel membrane. Hansen relates to a method of recovering nucleic acid by magnetic force, according to which magnetic beads and a sample liquid containing nucleic acid are mixed and agitated in a tube, to allow the beads to capture nucleic acid.

The subject matter of claims 28-31 would not have been obvious over Forsythe, Sauer and Hansen. Specifically, the Office Action fails to establish a *prima facie* case of obviousness. Courts have generally recognized that a showing of a *prima facie* case of obviousness necessitates three requirements: (i) some suggestion or motivation, either in the references themselves or in the knowledge of a person of ordinary skill in the art, to modify the reference or combine the reference teachings; (ii) a reasonable expectation of success; and (iii) the prior art references must teach or suggest all claim limitations. See e.g., In re Dembiczak, 175 F.3d 994 (Fed. Cir. 1999); In re Rouffet, 149 F.3d 1350, 1355 (Fed. Cir. 1998); Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc., 75 F.3d 1568, 1573 (Fed. Cir. 1996).

First, Forsythe, Sauer and Hansen, whether considered alone or in combination, do not disclose, teach or suggest all limitations of claims 28-31. Forsythe fails to disclose, teach or suggest "sucking and discharging the nucleic acid containing solution into and out of the tip by pressure change" or "contacting the nucleic acid containing solution with a solid phase" or "discharging air into the tip after discharging washing solution so that remaining liquid is discharged from the tip," as claim 28 recites. Forsythe uses the centrifugal separation method, according to which the solid phase to be used should have a high flow-through resistance so as to minimize the leakage of the sample liquid while setting on the column on the centrifuge, and not the

air-blowing technique to remove the remaining washing solution in the sucking/discharging method, as in the claimed invention.

In addition, Forsythe does not disclose "discharging the washing solution outside the tip" and "discharging air into the tip after discharging washing solution so that remaining liquid is discharged from the tip." In Forsythe, the sample liquid on or within the solid phase directly receives the centrifugal force. Accordingly, in Forsythe, little amount of the sample liquid will remain on or within the solid phase in the centrifugal separation method and, thus, Forsythe does not address the problem of the remaining washing solution. In fact, Forsythe does not even address nucleic acid recovery and, thus, the remaining washing solution problem cannot arise in the context of Forsythe.

Sauer also fails to disclose, teach or suggest all limitations of claims 28-31. Sauer is silent about "sucking and discharging the nucleic acid containing solution into and out of the tip by pressure change," much less about "contacting the nucleic acid containing solution with a solid phase" or "discharging air into the tip after discharging washing solution so that remaining liquid is discharged from the tip," as claim 28 recites. Sauer teaches a specific process for isolating circular nucleic acids from bacterial crude lysate by avoiding the need to form cleared lysate, and not the steps of the claimed invention.

Hansen is also silent about any of the limitations of claim 28. Hansen teaches using magnetic beads and a solid phase that contains nucleic acid capturing agent, so that the magnetic beads and a sample liquid containing nucleic acid are mixed and agitated in a tube to allow the beads to capture nucleic acids. Hansen also teaches that the magnetic beads, within which the nucleic acid is captured, are separated by magnetic force out of the mixture liquid in the tube.

Hansen fails to disclose "sucking and discharging the nucleic acid containing solution into and out of the tip by pressure change," much less "contacting the nucleic acid containing solution with a solid phase" or "discharging air into the tip after discharging washing solution so that remaining liquid is discharged from the tip," as in the claimed invention. The pipette tip in Hansen, which relies on Robot 104 and which would arguably correspond to the "tip" of the claimed invention, is a dispensing tip of an ordinary type, and not a tip that incorporates a solid phase containing nucleic acid capturing agent, as in the present invention.

Hansen also fails to disclose, teach or suggest "discharging the washing solution outside the tip" and "discharging air into the tip after discharging washing solution so that remaining liquid is discharged from the tip," as claim 28 recites. Hansen only mentions that robot 104 controls the positions of "pipette tips over a respective numbers of sample tubes 112" and then moves the pipette tips over to extractor 102 to release the samples into tubes 120 (col. 6, lines 43-49). Hansen is silent, however, about "discharging the washing solution outside the tip," much less about "discharging air into the tip after discharging washing solution so that remaining liquid is discharged from the tip." In fact, since the pipette tips of Hansen do not work in a manner similar to that of the tip defined in the present invention, the remaining washing solution problem cannot even arise in Hansen.

Second, a person of ordinary skill in the art would not have been motivated to combine Forsythe with Sauer or Hansen, to arrive at the subject matter of claims 28-31. Forsythe relates to an apparatus for separating fluids having a particular configuration. Forsythe specifically teaches "three pieces which may be nested together to form a stacked array." (Abstract). Sauer relates to a method of isolating circular nucleic acids from bacterial crude lysate to avoid the need to form cleared lysate. For

this, Sauer teaches a mixture "containing circular nucleic acids . . . treated under essentially alkaline conditions with a solid matrix consisting essentially of a silica material in presence of at least one chaotropic substance." (Col. 3, lines 20-24). Hansen relates to system for manipulating magnetically responsive particles of fluid samples to collect DNA or RNA from the sample. Hansen teaches that the system includes "heating and cooling devices . . . to release the nucleic acid molecules from the cells in the cell solution" and "movable magnets . . . to hold the magnetic responsive particles to which the nucleic molecules become bound." (Abstract).

A person skilled in the art would not have been motivated to combine the Forsythe apparatus, having three stacked pieces, with the Sauer system that requires specific alkaline conditions in presence of at least one chaotropic substance to allow purification of plasmid DNA without precipitation of cellular components and lysate clearing. One skilled in the art would also not have been motivated to employ the three-piece apparatus of Forsythe with the system of Hansen which requires heating and cooling devices as well as movable magnets, to manipulate magnetic and paramagnetic particles. Further, a person skilled in the art would not have been motivated to combine Forsythe and Sauer, which specifically use the centrifugal separation method, with Hansen, which specifically teaches a magnetic separation method.

Applicants also note that none of the cited references provides any description of, or suggestion for, the remaining washing solution problem, because all references fail to address sucking/discharging methods. Thus, none of the features of the air-blowing method as claimed in claim 28 can be derived from any of the centrifugal separation methods of Forsythe and Sauer, or from the magnetic separation method of Hansen. For at least these reasons, the Office Action fails to establish a *prima*

facie case of obviousness and withdrawal of the rejection of claims 28-31 is respectfully requested.

Allowance of all pending claims is solicited.

Dated: September 1, 2005

Respectfully submitted,

By Gabriela Coman

Mark J. Thronson
Registration No.: 33,082
Gabriela I. Coman
Registration No.: 50,515
DICKSTEIN SHAPIRO MORIN &
OSHINSKY LLP
2101 L Street NW
Washington, DC 20037-1526
(202) 785-9700
Attorneys for Applicants